Amendments to the Specification

Please replace the paragraphs on page 44, line 23 to page 46, line 4, i.e. Examples 14 and 15, with the following paragraphs:

EXAMPLE 14

Establishment of Polyclonal Antibodies Against HNOEL-iso

Polyclonal antibodies against two peptides located in the rat HNOEL polypeptide were raised by methods well known in the art:

~~***peptide***~~ ***Peptide 1:*** Ac-CQDQS SRHAA ELRDF KNK-NH_2, located at amino acid residues 44-61 (SEQ ID NO: 8);

Peptide 2: Ac-LDPQT LDTEQ QWDTP C-NH2, located at amino acid residues 301-316 (SEQ ID NO: 9).

EXAMPLE 15

Production and testing of siRNA against HNOEL-iso

We have identified (essentially using known methods as described above) and cloned siRNA sequences for HNOEL. The following 5 siRNA were cloned (all matching gi27660527 which is the rat HNOEL gene).

1. ~~5'-GATCCTGAAGCGGTTTGGT-3'~~

   5'-GAUCCUGAAGCGGUUUGGU-3' (SEQ ID NO: 3)

2. ~~5'-TGAGAAATACGATATGGTG-3'~~

   5'-UGAGAAAUACGAUAUGGUG-3' (SEQ ID NO: 4)

3. ~~5'-GATCTACGTGTTAGACGGC-3'~~

   5'-GAUCUACGUGUUAGACGGC-3' (SEQ ID NO: 5)

4. ~~5'-AGAAACTTGGCTAGACACAAA-3'~~

   5'-AGAAACUUGGCUAGACACAAA-3' (SEQ ID NO: 6)

5. ~~5'-AGATGGAAAATAGGAGAGTGC-3'~~

   5'-AGAUGGAAAAUAGGAGAGUGC-3' (SEQ ID NO: 7)

A series of experiments was performed using the above siRNAs:

A. **Expression of HNOEL:** In cells which express HNOEL endogenously (Ratl cells), it was shown that the expression of HNOEL was decreased 40-70% when any one of the above siRNAs was transiently transfected into the cells. This was determined on the mRNA level, as tested by semi-quantitative RT-PCR. These experiments were repeated with cells which over-express exogenous HNOEL (kidney epithelial cells strain 293) with essentially the same results.

B. **Proliferation rate:** Stable clones in Rat1 cells were established which expressed either siRNA #1 and siRNA #2 above (as verified by RT-PCR), resulting in reduction of approximately 50%-60% in HNOEL expression. It was shown that siRNA#1 and also

siRNA#2 expressing clones exhibited a reduction in proliferation rate as compared to the empty-vector transfected cells.

C. **TGF-beta treatment**: Normally, stimulation of Ratl cells with TGF-beta causes accumulation of fibronectin. The cells described in (B) above, i.e. siRNA #1 and siRNA#2 expressing cells, show reduction in fibronectin accumulation in response to TGF-beta stimulation, as observed both after 24 hr and 48hr following TGF-beta treatment, compared to the empty-vector cells.

These results strongly suggest that inhibition of HNOEL expression may have a beneficial effect on the development of fibrosis.

Similar methods to those described above may be used to produce siRNA to human HNOEL, and this siRNA may be used as a human therapeutic to treat fibrosis.

Sequence Listing:

Please replace the paper copy of the Sequence Listing filed with the subject application with the substitute paper copy of Sequence Listing attached hereto as **Exhibit B**.